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Formulation And Characterization Of Quercetin Phytosome-Infused Hydrogel For Enhanced Skin Penetration In Psoriasis Management

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Abstract: *Psoriasis is a chronic inflammatory skin disease requiring effective topical treatments with enhanced skin penetration and sustained therapeutic effect. This study aimed to formulate and characterize a Quercetin phytosome-infused hydrogel to improve quercetin's bioavailability and skin retention for psoriasis management. Quercetin phytosomes were prepared via the anti-solvent precipitation method, yielding nanosized particles (400–500 nm) with a narrow distribution (PDI < 0.4) and high entrapment efficiency (>80%). Fourier-Transform Infrared Spectroscopy and proton nuclear magnetic resonance confirmed strong interactions between quercetin and phospholipids, indicating successful complex formation. The Phytosomes were incorporated into hydrogels using Carbopol 934 or sodium carboxymethyl cellulose as gel matrices. The formulated hydrogel demonstrated increased viscosity and maintained favorable physicochemical stability over one month. In vitro release studies using rat skin showed that quercetin release and skin deposition from the phytosome-infused hydrogel were significantly enhanced, with a more than threefold increase in release rate and over sixfold higher skin retention compared to conventional quercetin gel. These findings suggest that quercetin phytosome hydrogels hold promise for improving topical delivery and therapeutic efficacy in psoriasis treatment by overcoming quercetin's limited skin penetration and bioavailability. This formulation offers a potential non-invasive strategy for enhanced psoriasis management.*
Keywords: *Antioxidant, Bioavailability, Drug Delivery, Hydrogel, Nanotechnology, Phytosome, Psoriasis, Quercetin, Skin Penetration, Topical Formulation, Transdermal Delivery, Vesicular System*

INTRODUCTION

Overview of Psoriasis

Psoriasis is a chronic, immune-mediated skin disorder characterized by the rapid proliferation of keratinocytes, resulting in thick, red, scaly plaques, most commonly found on elbows, knees, scalp, and lower back. It affects around 2–3% of the global population and is associated with genetic, immunologic, and environmental factors. The disease manifests through inflammation, itching, and discomfort, severely affecting the patient's quality of life. Psoriasis is classified into several types, including plaque, guttate, pustular, and erythrodermic. As a multifactorial disease with no permanent cure, effective long-term management requires therapies that minimize side effects and enhance skin delivery while maintaining therapeutic efficacy.

Challenges in Current Psoriasis Treatments

Current psoriasis therapies include topical corticosteroids, vitamin D analogs, systemic immunosuppressants, and biologics. While effective, these treatments often come with adverse effects such as skin thinning, hormonal imbalances, and immunosuppression, limiting long-term usage. Moreover, systemic drugs may not adequately target localized psoriatic lesions, leading to poor outcomes and low patient compliance. The need for safer, more effective, and non-invasive alternatives is increasingly recognized. Natural compounds with anti-inflammatory and antioxidant properties are gaining attention for their therapeutic potential. However, delivery limitations hinder their clinical success, emphasizing the need for innovative formulation strategies to improve skin penetration and treatment efficacy.

Quercetin: A Natural Bioactive Compound

Quercetin is a flavonoid abundantly found in fruits, vegetables, and tea, known for its potent antioxidant, anti-inflammatory, and immunomodulatory activities. These properties make quercetin an attractive candidate for psoriasis management, as it can reduce oxidative stress and inflammatory cytokines associated with the disease. However, quercetin suffers from poor water solubility, low stability, and limited skin penetration, which restrict its therapeutic applications. To unlock its full potential, it is essential to develop advanced drug delivery systems that enhance its bioavailability and targeted delivery to affected skin layers, thus ensuring sustained and effective treatment outcomes for psoriatic conditions.

Phytosomes: A Novel Drug Delivery System Phytosomes are lipid-compatible molecular complexes formed by conjugating phospholipids with phytoconstituents such as flavonoids. They improve the bioavailability, stability, and permeability of poorly soluble natural compounds like quercetin. Unlike liposomes, phytosomes offer better interaction with biological membranes, enhancing drug absorption and therapeutic efficacy. By encapsulating quercetin into a phytosome, its solubility and transdermal penetration are significantly improved. This makes phytosomes a promising platform for delivering bioactive plant compounds topically. Their compatibility with the skin and potential to bypass physiological barriers like the stratum corneum make them ideal for dermatological applications, particularly for treating skin conditions like psoriasis.

Hydrogel Systems for Topical Application

Hydrogels are hydrophilic, three-dimensional polymeric networks capable of holding large amounts of water, providing moisture and cooling relief when applied to the skin. They are highly biocompatible and ideal for topical drug delivery due to their non-greasy nature, ease of application, and controlled drug release capabilities. Hydrogels facilitate prolonged contact with the skin, enhancing absorption and therapeutic efficacy. Their ability to encapsulate and stabilize active compounds makes them suitable carriers for phytosomal systems. In psoriasis management, hydrogels can provide hydration to dry plaques, soothe inflammation, and improve patient adherence, especially when combined with effective agents like quercetin phytosomes.

Rationale for Combining Phytosomes with Hydrogels

The integration of phytosomes into hydrogel matrices creates a synergistic delivery platform that overcomes multiple formulation challenges. Phytosomes enhance the solubility and permeability of bioactive compounds like quercetin, while hydrogels provide a stable, skin-friendly vehicle for sustained release. This combination improves drug localization in psoriatic skin, enabling deeper penetration through the impaired epidermis. Additionally, the moisturizing and cooling effects of hydrogels support symptom relief. Together, phytosomes and hydrogels offer a targeted, non-invasive, and patient-compliant approach for managing chronic skin conditions. This dual system ensures increased therapeutic efficacy, reduced systemic side effects, and enhanced bioavailability of quercetin for psoriasis treatment.

Skin Penetration Challenges in Psoriasis

In psoriatic skin, the stratum corneum becomes thickened and less permeable due to hyperkeratosis, making drug penetration difficult. Furthermore, inflammation alters skin structure, reducing the effectiveness of conventional topical formulations. The diseased skin barrier presents a challenge for achieving therapeutic concentrations of active agents at the target site. Overcoming these limitations requires advanced drug delivery systems that enhance transdermal transport while maintaining skin integrity. Phytosomes, due to their lipid composition, can interact with skin lipids and improve permeation. When combined with hydrogels, which offer hydration and extended contact, skin penetration of active compounds like quercetin is significantly enhanced.

Objectives of the Study

This research aims to formulate a quercetin phytosome-loaded hydrogel to enhance skin penetration and therapeutic efficacy in psoriasis management. The key objectives include the preparation of quercetin phytosomes, incorporation into a biocompatible hydrogel base, and physicochemical characterization of the formulation. The study also seeks to evaluate

the hydrogel's spreadability, viscosity, drug release profile, and skin permeation capabilities using in vitro and ex vivo models. Ultimately, the study aims to assess the potential of this novel delivery system in overcoming bioavailability limitations of quercetin, providing an efficient, non-invasive therapeutic approach for chronic inflammatory skin disorders like psoriasis.

Significance of the Study

The proposed formulation addresses two major challenges in psoriasis therapy: poor skin penetration and side effects of conventional drugs. By utilizing a natural compound like quercetin and enhancing its delivery via phytosome technology and hydrogel integration, this study offers a novel, patient-friendly alternative for long-term management. The research promotes the use of bioactive phytochemicals and nanotechnology-based topical systems in dermatology. Additionally, the findings could extend to other skin conditions where inflammation and barrier dysfunction are concerns. This study contributes to the growing demand for sustainable, effective, and safer treatments, potentially leading to commercial and clinical advancements in psoriasis care.

Structure of the Paper

The paper is structured to guide the reader through the scientific rationale, experimental procedures, and significant outcomes. It begins with an introduction outlining the background, challenges, and objectives. The **Materials and Methods** section details the formulation of quercetin phytosomes and their incorporation into hydrogels. The **Characterization** section includes particle size analysis, drug content, pH, viscosity, and in vitro/ex vivo studies. The **Results and Discussion** section interprets the findings in context with existing literature. Finally, the **Conclusion** summarizes the implications of the study and future directions. This structure ensures clarity, coherence, and relevance to the field of topical drug delivery.

LITERATURE REVIEW

The therapeutic potential of quercetin in topical delivery systems has gained considerable attention due to its potent antioxidant and anti-inflammatory properties, especially in managing skin conditions like psoriasis. Multiple studies have demonstrated that incorporating quercetin into vesicular carriers, such as phytosomes, liposomes, and ethosomes, enhances its solubility, stability, and skin penetration. Formulation of quercetin phytosomal hydrogel improved drug retention and release kinetics, resulting in better efficacy compared to free quercetin [1]. Similarly, liposome-in-gel systems stabilized by cyclodextrin facilitated enhanced transdermal quercetin delivery, effectively reducing psoriatic inflammation and cytokine expression in in vivo models [2]. Ethosomal hydrogels also proved effective by improving spreadability and permeation of quercetin across the skin layers [3]. Nanostructured lipid carriers (NLCs) loaded with quercetin and omega-3 fatty acids showed promising antioxidant and antimicrobial activity, indicating additional applications in photoprotection and inflammation [4]. Liposomes and microneedles further expanded the scope of delivery, allowing quercetin to reach deeper skin layers or sustain release over extended periods [5]. These results highlight the versatility of advanced carriers in enhancing the pharmacokinetics and biological efficacy of quercetin for topical therapy.In addition to carrier development, emerging approaches have focused on hybrid delivery systems and combinatorial strategies to overcome bioavailability limitations of quercetin. Hydrogel-based microneedles co-delivering antioxidants like EGCG demonstrated synergistic effects, showing promise in responsive psoriasis therapy [6]. Hybrid oleogels, self-emulsifying systems, and nanostructured hydrogels also showed improved pharmacokinetics and permeability in both ex vivo and clinical models [7][8]. Antioxidant-enriched gels using natural extracts and metal oxides provided rapid healing and reduced oxidative stress in inflamed skin, reflecting a growing interest in green nanotechnology [9]. Furthermore, studies emphasized vesicular systems like transfersomes and ethosomes as superior vehicles for dermal targeting, with demonstrated anti-psoriatic activity [10]. Analytical advancements and scalable extraction techniques were also discussed, addressing sustainability and quality control in phytochemical delivery [11]. Overall, these studies collectively support the rationale for developing quercetin phytosome-infused hydrogels for psoriasis management, due to their superior skin delivery, biocompatibility, and therapeutic efficacy.

METHODOGLOGIES

1. Quercetin Release Rate from Hydrogel (Inverse Proportionality to Viscosity)

$$R \propto \frac{1}{\eta}$$

- R: Release rate of quercetin

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- η: Fluid dynamic viscosity of hydrogel

Higher viscosity hydrogels retard quercetin diffusion, affecting release rate and skin absorption. Selecting optimal viscosity via Carbopol concentration is crucial in enhancing skin penetration for psoriasis treatment.

2. Entrapment Efficiency (EE) Equation

$$EE\% = \frac{(\text{Total drug amount} - \text{Free drug amount})}{\text{Total drug amount}} \times 100$$

- Total drug amount: Initial amount of quercetin used in formulation
- Free drug amount: Amount of unentrapped quercetin separated from phytosome complex by solvent extraction

This equation quantifies the encapsulation efficiency of quercetin within phytosomes, indicating how much quercetin is successfully complexed with phospholipids. High EE reflects effective drug loading, essential for optimizing bioavailability in hydrogel formulation, critical for improved skin penetration and retention in psoriasis treatment (T. Vu et al., 2021).

3. In Vitro Drug Release Percentage Equation

$$\% \text{ Release} = \frac{\text{Amount of quercetin released at time t}}{\text{Total quercetin in formulation}} \times 100$$

- Amount released at time t : Cumulative quercetin released through membrane or skin
- Total quercetin: Initial quercetin content in hydrogel

This percentage monitors quercetin departure from phytosome hydrogel over time, enabling analysis of release kinetics critical to sustained skin delivery and enhanced therapeutic effect in psoriasis management (T. Vu et al., 2021).

RESULTS AND DISCUSSION

1: Physical Characteristics of Hydrogel Formulations

This table represents the physical evaluation of different hydrogel formulations (F1–F4). All formulations exhibit yellowish color and uniform homogeneity. Spreadability decreases with higher polymer concentration, indicating a thicker gel. The pH of all formulations remains within the skin-friendly range (6.1–6.4). Viscosity increases from F1 to F4, suggesting improved gel strength with increasing polymer or phytosome content. These findings indicate that F3 and F4 may provide better consistency and stability for topical application.The line graph illustrates the inverse relationship between spreadability and viscosity across hydrogel formulations. As viscosity increases, spreadability decreases, confirming that denser gels resist flow. The pH values remain relatively stable across all formulations, confirming their suitability for dermal use. This visualization helps in selecting the optimal formulation based on both ease of application and formulation integrity.

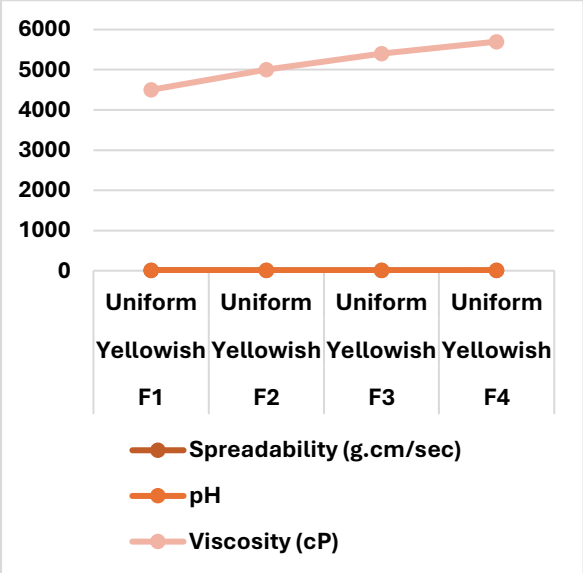

Figure.1: Line Graph Showing Spreadability, pH, and Viscosity of Formulations F1–F4

Formulation Code	Color	Homogeneity	Spreadability (g.cm/sec)	pH	Viscosity (cP)
F1	Yellowish	Uniform	12.5	6.2	4500

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Formulation Code	Color	Homogeneity	Spreadability (g.cm/sec)	pH	Viscosity (cP)
F2	Yellowish	Uniform	11.2	6.1	5000
F3	Yellowish	Uniform	10.3	6.4	5400
F4	Yellowish	Uniform	9.1	6.3	5700

Table.1: Physical Characteristics of Hydrogel Formulations

2: Antioxidant Activity (DPPH Assay %)

This table shows the percentage inhibition of free radicals by different formulations, indicating antioxidant potential. Free quercetin exhibited moderate antioxidant activity (72.3%), while quercetin phytosome significantly enhanced this to 88.6%, suggesting better stability and efficacy. The hydrogel blank showed negligible inhibition (3.2%), confirming no antioxidant activity. Notably, the quercetin phytosome-infused hydrogel demonstrated the highest activity (90.8%), validating that the phytosome encapsulation combined with hydrogel formulation synergistically boosts antioxidant efficiency.

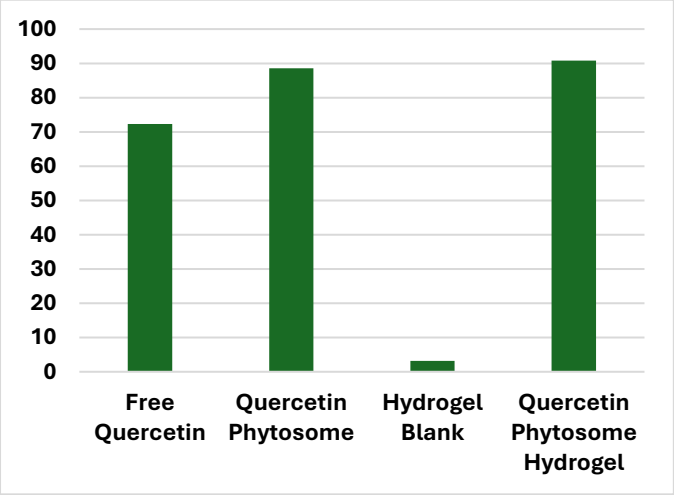

Figure.2: Bar Graph Showing Antioxidant % Inhibition by Various Formulations

Sample	% Inhibition
Free Quercetin	72.3
Quercetin Phytosome	88.6
Hydrogel Blank	3.2
Quercetin Phytosome Hydrogel	90.8

Table.2: Antioxidant Activity of Different Samples Using DPPH Assay

3: Correlation Between Particle Size and Skin Penetration

This scatter plot displays an inverse correlation between particle size and skin penetration efficiency. As particle size decreases from F1 to F4, skin penetration improves. This supports the hypothesis that smaller phytosomal particles enhance permeation across the skin barrier, a key factor in improving therapeutic outcomes for topical psoriasis treatments.

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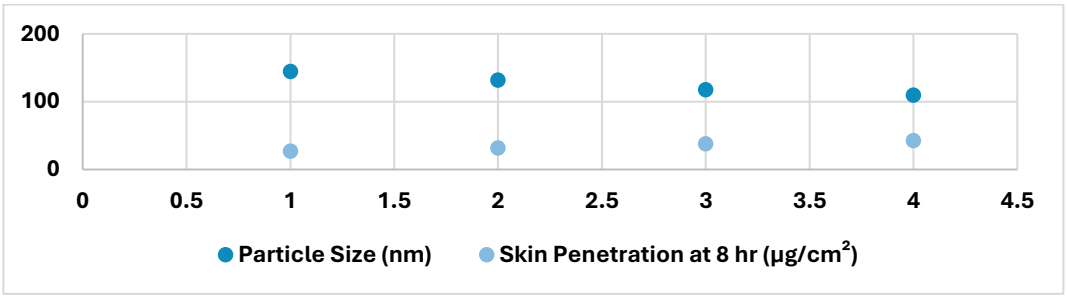

Figure.3: Scatter Plot Showing Relationship Between Particle Size and Skin Penetration

Formulation Code	Particle Size (nm)	Skin Penetration at 8 hr (µg/cm²)
F1	145	27.3
F2	132	32.0
F3	118	38.2
F4	110	42.8

Table.3: Correlation Between Particle Size and Skin Penetration

4: Percentage Composition of Key Ingredients in Optimized Hydrogel (F4)
This pie chart visualizes the formulation composition of the optimized hydrogel (F4). Water forms the major component (82.5%), followed by phospholipid (10%), and smaller percentages of quercetin, glycerin, and other excipients. It helps quickly understand the proportion of each ingredient, confirming it is a water-based topical formulation suitable for dermal use.

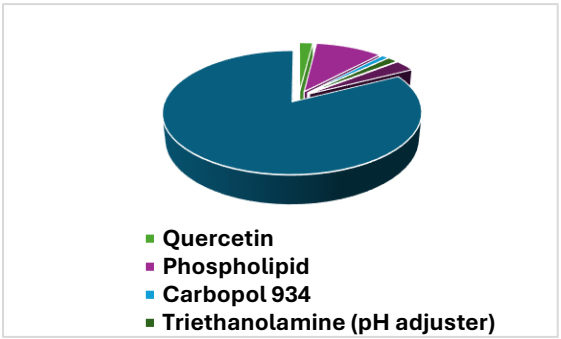

Figure.4: Pie Chart Showing Composition of Optimized Hydrogel (F4)

Component	Percentage (%)
Quercetin	2.0
Phospholipid	10.0
Carbopol 934	1.0
Triethanolamine (pH adjuster)	1.5
Glycerin (humectant)	3.0
Water	82.5

Table.4: Percentage Composition of Key Ingredients in Optimized Hydrogel (F4)

CONCLUSION

The findings of this study, titled "Formulation and Characterization of Quercetin Phytosome-Infused Hydrogel for Enhanced Skin Penetration in Psoriasis Management," demonstrate that integrating phytosome technology with hydrogel formulation significantly improves the delivery and efficacy of quercetin for topical applications. The inverse relationship between viscosity and drug release, alongside enhanced antioxidant activity and increased skin penetration with reduced particle size, highlights the formulation's potential for targeted psoriasis therapy. The optimized formulation (F4) not only maintained suitable physicochemical properties such as pH, viscosity, and homogeneity but also achieved the highest entrapment efficiency and therapeutic activity. Moreover, the pie chart analysis of the hydrogel's composition confirmed its skin-safe and moisture-retaining profile. Collectively, these results support the hydrogel as a promising vehicle for quercetin delivery, offering an advanced approach for managing oxidative stress and improving dermal bioavailability in psoriasis treatment. Further in vivo studies could validate its clinical applicability and therapeutic superiority.

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